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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,730	04/14/2004	Sunghoon Kim	058333-0118	5013

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EXAMINER	
LIETO, LOUIS D	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 09/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/823,730	KIM ET AL.	
	Examiner	Art Unit	
	Louis D Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

The specification on page 5 lists Figures 1-4 in the brief description of the drawings. However, the descriptions of drawings 1-3 describe material, which is not present in the drawings of Figures 1-3. Specifically, the drawings of Figures 1-3 are all exact duplicates of Figure 4, as described in the brief description of drawings. Applicant is required to amend the brief description of drawings to reflect the actual drawings submitted and remove all references to the missing drawings. See MPEP 601.01(g).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the induction of TNF and Il-18 in a monocytic leukemia cell line, *in vitro*, does not reasonably provide enablement for an enhancement of any type of immune response in any cell or tissue, *in vitro* or *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to perform the invention commensurate in scope with these claims.

The specification does not provide guidance on the enhancement of any type of immune response in any cell or tissue. The working examples teach that polypeptides SEQ ID NO: 1 or

SEQ ID NO: 2 can induce IL-8 and TNF production from THP-1 cells, a monocytic leukemia cell line. The specification states that the immunological enhancement agent is comprised in the N-terminal domain of p43, e.g. polypeptides SEQ ID NO: 1 or SEQ ID NO: 2 (Specification, pg. 4 pgph 3). However, the prior art of record attributes the cytokine activity to p43's C-terminus cleavage product EMAP II {Norcum et al. (2000) J. Bio. Chem. 275:17921-17924; pg. 17921, col. 2, pgph 2}. Norcum et al. teaches, "EMAP II leads to acute inflammation and...sensitizes tumors to tumor necrosis factor α" (Norcum et al. pg. 17921, col. 2, pgph 2). The art does not teach that polypeptides SEQ ID NO: 1 or SEQ ID NO: 2 can enhance any immune response.

Further, a method of enhancing an immune response in any cell or tissue is overly broad since the specification fails to disclose that culture with the polypeptide SEQ ID NO: 1 or SEQ ID NO: 2 and any cell or tissue type causes the release of any cytokine, other than IL-8 or TNF from THP-1 cells. The specification fails to provide guidance on the induction of any other immune response, such as degranulation, antibody production, chemotaxis, or proliferation. Certain immune responses are cell type specific, such as B cell production of antibodies, which makes it impossible to extrapolate on the enhancement of any and all immune responses based on cytokine secretion from a monocytic cell line {Abbas et al., (1994) Cellular and Molecular Immunology 2nd ed., 1-457; pg. 75, col. 2, pgph 3}. The polypeptides SEQ ID NO: 1 or SEQ ID NO: 2 are not known in the art to enhance any immune response in any cell or tissue.

In addition, the specification does not teach that the polypeptides SEQ ID NO: 1 or SEQ ID NO: 2 can enhance any type of immune response *in vivo*. As discussed above, the working examples in the specification are confined to THP-1 cells, a monocytic leukemia cell line. The examples teach that THP-1 cells can be induced, *in vitro,* to increase TNF and IL-8 production in

response to stimulation with the polypeptides SEQ ID NO: 1 or SEQ ID NO: 2. Ross et al. teaches that "Cell line studies, however, must be interpreted in the context of artifacts introduced by selection and establishment of cell lines *in vivo*" {Ross et al. (2001) Disease Markers 17:99-109; pg. 99, Abstract}. Ross et al. further provides that in the field of tumor biology this has led to difficulties extrapolating biology observed in cell lines to tumor biology *in vivo* (Ross et al., pg. 99, Abstract). Thus, based on the lack of teachings in the art at the time of filing that polypeptides SEQ ID NO: 1 or SEQ ID NO: 2 could enhance any immune response in any cell or tissue, the art acknowledged unpredictability of prognosticating *in vivo* outcomes based on *in vitro* results, and the complete lack of guidance in the specification concerning how to enhance any and all immune responses through administration of polypeptides SEQ ID NO: 1 or SEQ ID NO: 2 to any cell or tissue, a skilled practitioner would be unable to determine how to enhance any immune response in any cell or tissue, other than to increase TNF or IL-8 production in a monocytic leukemia cell line, *in vitro*, without arduous and extensive experimentation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4 and 5 of copending Application No. US 09/930,169. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 4 and 5 of U. S. Patent Application No: US 09/930,169 are species of the broader genus of claim1 in the instant application. Specifically, claim 1 of the instant application is to a method of enhancing an immune response comprising administering to a cell or tissue a polypeptide consisting of SEQ ID NO: 1 or SEQ ID NO: 2. Claim 4 of U. S. Patent Application No: US 09/930,169 reads on a method of inducing IL-8 production comprising administering the agent of claim 1, which is an immunological enhancement agent comprising a polypeptide consisting of SEQ ID NO: 1 or SEQ ID NO: 2, to a cell or tissue. Claim 5 of U. S. Patent Application No: US 09/930,169 reads on a method of inducing TNF production comprising administering the agent of claim 1 to a cell or tissue. IL-8 and TNF are known in the art to be cytokines that are effective regulators of the immune system. Therefore, the pending claims render the instant claim 1 obvious. It is well established that a species of a claimed invention renders the genus obvious In re Schaumann, 572 F.2d 312, 197 USPQ 5 (CCPA 1978).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Please note that the closest prior art is exemplified by Kao et al. Kao et al.{Kao et al. (1994) J. Biol. Chem. 269:25106-25119}. Kao et al. teaches the full length p43 peptide

(SwissProt AC Q12904) and as such does not read on the p43 fragments of SEQ ID NO: 1 or SEQ ID NO: 2.

Claim 1 is free of the prior art of record

No Claims allowed

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy J Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703)-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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